RENAL PHYSIOLOGY AND KIDNEY STONES

TO032 KIDNEY STONES AND CARDIOVASCULAR EVENTS: A COHORT STUDY
R. Todd Alexander1, Susan Samuel1, Natasha Weibel1, Aminu Bello1, Scott Klarenbach1, Gary C. Curhan1, Marcello Tonelli1 and Brenda Hemmelgarn1
1Alberta Kidney Disease Network Alberta Canada

Introduction and Aims: Kidney stone formers share some common risk factors associated with the development of atherosclerosis including diabetes and hypertension. However, whether having a kidney stone is associated with increased risk of cardiovascular events is uncertain.

Methods: We studied 3,897,684 people aged ≥18 years and living in Alberta Canada between 1997 and 2009, excluding those on dialysis or with a kidney transplant at baseline. Individuals who developed one or more kidney stone were identified from claims and facility utilization data. We compared the risk of incident acute myocardial infarction (AMI), death due to coronary heart disease (CHD), percutaneous transluminal coronary angioplasty (PTCA)/coronary bypass surgery (CABG) or stroke between stone formers and non-stone formers.

Results: During median follow-up of 11y, 25,532 (0.8%) participants had at least one kidney stone, 28,455 (0.9%) had an AMI, 34,643 (1.1%) died of CHD, 28,539 (0.9%) underwent PTCA or CABG, and 16,697 (0.5%) had a stroke. In total, 87,262 (3%) individuals had at least one cardiovascular event during follow-up. Compared to people without kidney stones, people who had at least one kidney stone during follow-up had an increased risk of subsequent AMI (adjusted HR 1.35, 95% CI 1.21, 1.50), PTCA/CABG (HR 1.62, 95% CI 1.46, 1.81) and an increased risk of subsequent AMI (adjusted HR 1.54, 95% CI 1.38, 1.72), CHD death (HR 1.62, 95% CI 1.21, 1.50), PTCA/CABG (HR 1.46, 1.81) and stroke (HR 1.35, 95% CI 1.15, 1.58). The magnitude of the excess risk associated with a kidney stone appeared more pronounced for younger people (compared to older people, p<0.001) and women (vs men, p=0.01). These data suggest that people with a clinically recognized kidney stone should be followed more closely to evaluate for the possibility of subsequent cardiovascular events – younger people and women.

TO032 Figure 1:

TO033 CALCIUM SENSING RECEPTOR INFLUENCES THE EXPRESSION OF CLAUDIN 14 IN LOOP OF HENLE THICK ASCENDING TRACT
Alessandra Mingione1, Annalisa Terranegra1, Andrea Alojia1, Teresa Arcidiacono2, Caterina Branzano1, Jianghui Hou1, Giacomo Dell’Antono2, Giuseppe Vezzoli3 and Laura Soldati1
1Milan University Milano Italy, 2S. Raffaele Hospital Milano Italy, 3Washington University St Louis MO United States

Introduction and Aims: The calcium-sensing receptor (CaSR) is a membrane protein activated by extracellular calcium and expressed throughout the renal tubule. In the thick ascending limb of Henle tract (Talh) the CaSR inhibits the reabsorption of calcium through its regulatory action on claudin 14 (CLDN14) that blocks the channel for the transport of calcium into the intercellular junctions (tight junctions), favoring the excretion of calcium and hypercalciuria. It was observed that mice with reduced expression of CaSR showed a downregulation of CLDN14. To demonstrate in humans the relationship between the two molecules, we evaluated the expression of CaSR and CLDN14 in 104 human renal medullary tissue samples.

Methods: The sample was obtained from normal non-neoplastic tissue immediately after the nephrectomy. The expression of CaSR and CLDN14 was measured as mRNA and was normalized to the mRNA of glyceraldehyde-3-phosphate dehydrogenase (GAPDH). The total mRNA was extracted from 10-30 mg of renal tissue. The mRNA of CaSR, CLDN14 and GAPDH were measured using SYBR-Green Real-Time PCR of 100 ng of cDNA using specific primers. It was also done genotyping of DNA extracted from the samples for the polymorphism rs6776158 A>G of the CaSR gene 1 promoter by the specific genotyping assay.

Results: The transcriptional activity of the promoter 1 CaSR gene in the presence of alleles of the polymorphism rs6776158 A>G has been previously tested in HEK293 cells transfected with a plasmid containing the promoter 1 and the luciferase gene. The results in this in-vitro system have shown that the minor G allele of rs6776158 causes a decrease of the promoter transcriptional efficiency and a reduced expression of CaSR. In renal medulla tissue, the expression (mRNA) of CaSR was higher in patients carrying the A allele (n=92) compared to homozygotes for the minor G allele (n=12; 1.1±0.58 vs. 0.58±0.74 vs. vm ± SD, p=0.048). The expression of CLDN14 was higher in patients carrying the A allele compared to homozygotes for the minor G allele (2.21±0.22 vs 1.69±1.17, p=0.018). The expression of CLDN14 was positively correlated with that of the CaSR in renal medullary tissue (r=0.40, p=0.0001).

Conclusions: The reduction of CaSR expression is associated with a reduced expression of CLDN14, favoring the renal reabsorption of calcium in Talh. The CaSR seems then adjust the excretion of calcium through the control of the expression of CLDN14 in Talh. Inactivating the promoter polymorphisms of the CaSR can protect from hypercalciuria through activation of paracellular reabsorption in Talh.

TO034 POSSIBLE CORRELATION OF DOWN-REGULATED CLAUDIN-16, TIGHT JUNCTION MOLECULE IN TAL, WITH LOWERED MAGNESIUM REABSORPTION ASSOCIATED WITH TUBULO-INTERSTITIAL NEPHROPATHY
Taisuke Shimizu1, Hajime Hasegawa1, Kaori Takayanagi1,2, Akira Ikari3, Chie Noiri1, Takatsugu Iwashita1, Yosuke Tayama1, Juko Asakura1, Naohiko Anzai4, Tatsuro Sano1, Tomonari Ogawa1, Akihiko Matsuda1 and Tetsuya Mitarai1
1Dept of Nephrol & Hypertens Saitama Med Center, Saitama Med Univ Kawagoe Japan, 2Kawagoe Exmrc Clinic Kawagoe Japan, 3Pharmaco-Biochemistry School of Pharmaceutical Sciences, University of Shizuoka Shizuoka Japan, 4Pharmacology and Toxicology Dokkyo Medical University School of Medicine Tochigi Japan

Introduction and Aims: Hypermagnesiuria has been considered as a characteristic pathological setting in tubulo-interstitial nephropathy (TIN) although its underlying mechanisms has not been understood. The aim of this work was to elucidate the molecular profile of Mg transporting molecules in TIN by use of unilateral ureter obstruction (UUO) model which showed glomerular injury-independent TIN.

Methods: Left kidney was sampled at day-0, 1 and 7 after ligation of left ureter of male SD rats. For the assessment of TIN and changes in the expressions of Mg transporting molecules in TIN by use of unilateral ureter obstruction (UUO) model which showed glomerular injury-independent TIN.

Results: Fractional excretion of Mg was increased at day-7 but not at day-1 (3.10±0.8% at day-0, 4.62±0.5% at day-1, 10.7±0.8% at day-7). Gene expression of claudin-16, tight junctional pathway of Mg at mTAL, was also decreased at day-7 but not at day-1 (100.3

© The Author 2013. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com
null
null